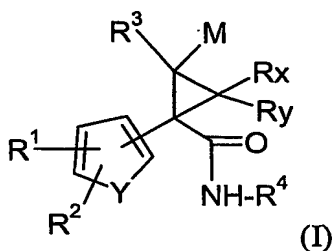


-126-

CLAIMS

1. A compound of the formula



wherein

Y is $-\text{CH}=\text{CH}-$, $-\text{CH}=\text{N}-$, sulfur or oxygen; and

M is hydrogen, halo, lower alkyl, or perfluoro lower alkyl; and

- 10 Rx and Ry are hydrogen, halo or methyl; and

R^1 and R^2 are independently hydrogen, halo, amino, hydroxyamino, nitro, cyano, sulfonamido, lower alkyl, $-\text{OR}^5$, $-\text{COOR}^5$, perfluoro- lower alkyl, lower alkyl thio, perfluoro-lower alkyl thio, lower alkyl sulfonyl, perfluoro lower alkyl sulfonyl, lower alkyl sulfinyl,

- 15 R^5 is hydrogen, lower alkyl or perfluoro-lower alkyl; or furthermore

R^1 , R^2 can be $-(\text{CH}_2)_n-\text{NR}^6\text{R}^7$, with $n=1, 2, 3$ or 4 and

R^6 and R^7 are independently hydrogen or lower alkyl; or together with the nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-

- 20 membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen; or

R^1 , R^2 can be alkynyl,

substituted with hydrogen, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, an unsubstituted or hydroxy substituted cycloalkyl ring containing 5 or 6 carbon atoms, a

- 25 five- or six-membered saturated heterocyclic ring which contains from 1 to 3 hetero atoms selected from the group consisting of sulfur, oxygen or nitrogen, or an unsubstituted five- or six-membered heteroaromatic ring, connected by a ring carbon atom, which contains from 1 to 3 heteroatoms in the ring selected from the group consisting of sulfur, nitrogen and oxygen, or $-(\text{CH}_2)_n-\text{NR}^8\text{R}^9$, with $n=1, 2$, and

-127-

- R^8 and R^9 are independently hydrogen or lower alkyl; or together with the nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen; or
- R^1 , R^2 can be $R^{10}-(CH_2)_y-W]z-$, with
- W is oxygen, sulfur, $-SO-$, $-SO_2-$, and
- R^{10} is a heteroaromatic ring, connected by a ring carbon atom, which contains from 5 to 6 ring members with from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur or nitrogen, or
- aryl containing 6 or 10 ring carbon atoms, or
- aryl containing from 6 ring carbon atoms fused with a heteroaromatic ring containing 5 or 6 ring members with 1 or 2 heteroatoms in the ring being selected from the group consisting of nitrogen, oxygen or sulfur, or
- a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, or
- a cycloalkyl ring having 5 or 6 carbon atoms, or
- $-NR^{11}R^{12}$, with R^{11} and R^{12} are independently hydrogen or lower alkyl;
- y is independently 0, 1, 2, 3 or 4; z is independently 0, 1; or
- R^1 , R^2 can be $R^{13}-(CH_2)_t-U-$, with
- U is $-NHCO-$, $-CONH-$, $-NHSO_2-$, $-SO_2NH-$ and
- R^{13} in the same meaning of R^{10} and
- perfluoro-lower alkyl, lower alkyl, lower alkoxy carbonyl or
- $-NR^{14}R^{15}$, R^{14} and R^{15} are independently hydrogen or lower alkyl; or together with the nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-membered heterocycloalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen;
- t is an integer being 0, 1, 2, 3 or 4;
- R^3 is lower alkyl or halo lower alkyl having from 2 to 6 carbon atoms or arylalkyl or $-(CH_2)_s-V$ where V is a 3 to 8-membered ring which is cycloalkyl, cycloalkenyl, or heterocycloalkyl having one heteroatom selected from oxygen and sulfur;

-128-

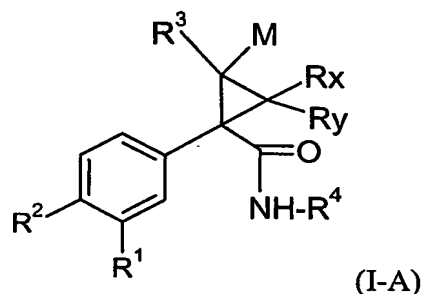
s is independently 0, 1 or 2;

R^4 is $-C(O)NHR^{16}$, or is R^{17} ;

R^{16} is hydrogen, lower alkyl, lower alkenyl, hydroxy lower alkyl,
 $-(CH_2)_n-COOR^{18}$, $-CO-(CH_2)_n-COOR^{19}$;

- 5 R^{17} is an unsubstituted, mono- or di-substituted five- or six-membered heteroaromatic ring connected by a ring carbon atom to the amide group shown, which five- or six-membered heteroaromatic ring contains from 1 to 4 heteroatoms selected from sulfur, oxygen or nitrogen, with one heteroatom being nitrogen which is adjacent to the connecting ring carbon atom; said mono- or di-substituted heteroaromatic ring being mono- or di-
- 10 substituted at a position on a ring carbon atom other than adjacent to said connecting carbon atom with a substituent selected from the group consisting of lower alkyl, halo, nitro, cyano, $-(CH_2)_n-OR^{20}$, $-(CH_2)_n-COOR^{21}$,
 $-(CH_2)_n-CONHR^{22}$, $-(CH_2)_n-NHR^{23}$,
 n is 0, 1, 2, 3 or 4;
- 15 R^{18} , R^{19} , R^{20} , R^{21} , R^{22} and R^{23} are independently hydrogen or lower alkyl, and its pharmaceutically acceptable salts thereof.

2. A compound according to claim 1 having the formula



wherein

M is hydrogen, halo, lower alkyl or perfluoro lower alkyl; and

Rx and Ry are hydrogen, halo or methyl; and

- 25 R^1 and R^2 are independently hydrogen, halo, amino, hydroxyamino, nitro, cyano, sulfonamido, lower alkyl, $-OR^5$, $-COOR^5$, perfluoro- lower alkyl, lower alkyl thio, perfluoro-lower alkyl thio, lower alkyl sulfonyl, perfluoro lower alkyl sulfonyl, lower alkyl sulfinyl,

-129-

R⁵ is hydrogen, lower alkyl or perfluoro-lower alkyl; or furthermore

R¹, R² can be $-(CH_2)_n-NR^6R^7$, with n=1, 2, 3 or 4 and

R⁶ and R⁷ are independently hydrogen or lower alkyl; or together with the nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen; or

R¹, R² can be alkynyl,

substituted with hydrogen, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, an unsubstituted or hydroxy substituted cycloalkyl ring containing 5 or 6 carbon atoms, a five- or six-membered saturated heterocyclic ring which contains from 1 to 3 hetero atoms selected from the group consisting of sulfur, oxygen or nitrogen, or an unsubstituted five- or six-membered heteroaromatic ring, connected by a ring carbon atom, which contains from 1 to 3 heteroatoms in the ring selected from the group consisting of sulfur, nitrogen and oxygen, or $-(CH_2)_n-NR^8R^9$, with n=1, 2, and

R⁸ and R⁹ are independently hydrogen or lower alkyl; or together with the nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen; or

R¹, R² can be $R^{10}-[(CH_2)_y-W]_z-$, with

W is oxygen, sulfur, $-SO-$, $-SO_2-$, and

R¹⁰ is a heteroaromatic ring, connected by a ring carbon atom, which contains from 5 to 6 ring members with from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur or nitrogen, or

aryl containing 6 or 10 ring carbon atoms, or

aryl containing from 6 ring carbon atoms fused with a heteroaromatic ring containing 5 or 6 ring members with 1 or 2 heteroatoms in the ring being selected from the group consisting of nitrogen, oxygen or sulfur, or

a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, or a cycloalkyl ring having 5 or 6 carbon atoms, or

-130-

-NR¹¹R¹², with R¹¹ and R¹² are independently hydrogen or lower alkyl;

y is independently 0, 1, 2, 3 or 4; z is independently 0, 1; or

R¹, R² can be R¹³-(CH₂)_t-U-, with

U is -NHCO-, -CONH-, -NHSO₂-, -SO₂NH- and

5 R¹³ in the same meaning of R¹⁰ and

perfluoro-lower alkyl, lower alkyl, lower alkoxycarbonyl or

-NR¹⁴R¹⁵, R¹⁴ and R¹⁵ are independently hydrogen or lower alkyl; or together with the

nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated

10 5- or 6- membered heterocycloalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen;

t is an integer being 0, 1, 2, 3 or 4;

R³ is lower alkyl or halo lower alkyl having from 2 to 6 carbon atoms or arylalkyl or -

(CH₂)_s-V where V is a 3 to 8-membered ring which is cycloalkyl, cycloalkenyl, or

15 heterocycloalkyl having one heteroatom selected from oxygen and sulfur;

s is independently 0, 1 or 2;

R⁴ is -C(O)NHR¹⁶, or is R¹⁷;

R¹⁶ is hydrogen, lower alkyl, lower alkenyl, hydroxy lower alkyl,

-(CH₂)_n-COOR¹⁸, -CO-(CH₂)_n-COOR¹⁹;

20 R¹⁷ is an unsubstituted, mono- or di-substituted five- or six-membered heteroaromatic ring connected by a ring carbon atom to the amide group shown, which five- or six-membered heteroaromatic ring contains from 1 to 4 heteroatoms selected from sulfur, oxygen or nitrogen, with one heteroatom being nitrogen which is adjacent to the connecting ring carbon atom; said mono- or di-substituted heteroaromatic ring being mono- or di-

25 substituted at a position on a ring carbon atom other than adjacent to said connecting carbon atom with a substituent selected from the group consisting of lower alkyl, halo, nitro, cyano, -(CH₂)_n-OR²⁰, -(CH₂)_n-COOR²¹,

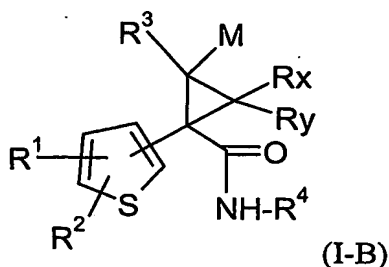
-(CH₂)_n-CONHR²², -(CH₂)_n-NHR²³,

n is 0, 1, 2, 3 or 4;

30 R¹⁸, R¹⁹, R²⁰, R²¹, R²² and R²³ are independently hydrogen or lower alkyl, and its pharmaceutically acceptable salts thereof.

-131-

3. A compound according to claim 1 having the formula



wherein

- 5 M is hydrogen, halo, lower alkyl or perfluoro lower alkyl; and
 Rx and Ry are hydrogen, halo or methyl; and
 R¹ and R² are independently hydrogen, halo, amino, hydroxyamino, nitro,
 cyano, sulfonamido, lower alkyl, -OR⁵, -COOR⁵, perfluoro- lower alkyl, lower
 alkyl thio, perfluoro-lower alkyl thio, lower alkyl sulfonyl, perfluoro lower
 10 alkyl sulfonyl, lower alkyl sulfinyl,
 R⁵ is hydrogen, lower alkyl or perfluoro-lower alkyl; or furthermore
 R¹, R² can be -(CH₂)_n-NR⁶R⁷, with n=1, 2, 3 or 4 and
 R⁶ and R⁷ are independently hydrogen or lower alkyl; or together with the nitrogen atom
 to which they are attached form a five or six-membered heteroaromatic ring containing
 15 from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-
 membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from
 the group consisting of oxygen, sulfur and nitrogen; or
 R¹, R² can be alkynyl,
 substituted with hydrogen, lower alkyl, hydroxy lower alkyl, lower alkoxy lower alkyl, an
 20 unsubstituted or hydroxy substituted cycloalkyl ring containing 5 or 6 carbon atoms, a
 five- or six-membered saturated heterocyclic ring which contains from 1 to 3 hetero atoms
 selected from the group consisting of sulfur, oxygen or nitrogen, or an unsubstituted five-
 or six-membered heteroaromatic ring, connected by a ring carbon atom, which contains
 from 1 to 3 heteroatoms in the ring selected from the group consisting of sulfur, nitrogen
 25 and oxygen, or -(CH₂)_n-NR⁸R⁹, with n=1, 2, and
 R⁸ and R⁹ are independently hydrogen or lower alkyl; or together with the nitrogen atom
 to which they are attached form a five or six-membered heteroaromatic ring containing
 from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated 5- or 6-

-132-

membered cycloheteroalkyl ring, which contains from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen; or

R^1, R^2 can be $R^{10}-[(CH_2)_y-W]_z-$, with

W is oxygen, sulfur, $-SO-$, $-SO_2-$, and

- 5 R^{10} is a heteroaromatic ring, connected by a ring carbon atom, which contains from 5 to 6 ring members with from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur or nitrogen, or

aryl containing 6 or 10 ring carbon atoms, or

aryl containing from 6 ring carbon atoms fused with a heteroaromatic ring containing 5 or

- 10 6 ring members with 1 or 2 heteroatoms in the ring being selected from the group consisting of nitrogen, oxygen or sulfur, or

a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2

heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, or

a cycloalkyl ring having 5 or 6 carbon atoms, or

- 15 $-NR^{11}R^{12}$, with R^{11} and R^{12} are independently hydrogen or lower alkyl;

y is independently 0, 1, 2, 3 or 4; z is independently 0, 1; or

R^1, R^2 can be $R^{13}-(CH_2)_t-U-$, with

U is $-NHCO-$, $-CONH-$, $-NHSO_2-$, $-SO_2NH-$ and

R^{13} in the same meaning of R^{10} and

- 20 perfluoro-lower alkyl, lower alkyl, lower alkoxy carbonyl or

$-NR^{14}R^{15}$, R^{14} and R^{15} are independently hydrogen or lower alkyl; or together with the

nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring

containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen; or a saturated

5- or 6- membered heterocycloalkyl ring, which contains from 1 to 2 heteroatoms selected

- 25 from the group consisting of oxygen, sulfur and nitrogen;

t is an integer being 0, 1, 2, 3 or 4;

R^3 is lower alkyl or halo lower alkyl having from 2 to 6 carbon atoms or arylalkyl or

$(CH_2)_s-V$ where V is a 3 to 8-membered ring which is cycloalkyl, cycloalkenyl, or

heterocycloalkyl having one heteroatom selected from oxygen and sulfur;

- 30 s is independently 0, 1 or 2;

R^4 is $-C(O)NHR^{16}$, or is R^{17} ;

R^{16} is hydrogen, lower alkyl, lower alkenyl, hydroxy lower alkyl,

-133-

$-(CH_2)_n-COOR^{18}$, $-CO-(CH_2)_n-COOR^{19}$;

R^{17} is an unsubstituted, mono- or di-substituted five- or six-membered heteroaromatic ring connected by a ring carbon atom to the amide group shown, which five- or six-membered heteroaromatic ring contains from 1 to 4 heteroatoms selected from sulfur, oxygen or

5 nitrogen, with one heteroatom being nitrogen which is adjacent to the connecting ring carbon atom; said mono- or di-substituted heteroaromatic ring being mono- or di-substituted at a position on a ring carbon atom other than adjacent to said connecting carbon atom with a substituent selected from the group consisting of lower alkyl, halo, nitro, cyano, $-(CH_2)_n-OR^{20}$, $-(CH_2)_n-COOR^{21}$,

10 $-(CH_2)_n-CONHR^{22}$, $-(CH_2)_n-NHR^{23}$,

n is 0, 1, 2, 3 or 4;

R^{18} , R^{19} , R^{20} , R^{21} , R^{22} and R^{23} are independently hydrogen or lower alkyl, and its pharmaceutically acceptable salts thereof.

15 4. A compound according to any one of claims 1 to 3, wherein

R^4 is an unsubstituted, mono- or di-substituted five- or six-membered heteroaromatic ring connected by a ring carbon atom to the amide group shown, which five- or six-membered heteroaromatic ring contains from 1 to 4 heteroatoms selected from sulfur, oxygen or nitrogen, with one heteroatom being nitrogen which is adjacent to the connecting ring

20 carbon atom; said mono- or di-substituted heteroaromatic ring being mono- or di-substituted at a position on a ring carbon atom other than adjacent to said connecting carbon atom with a substituent selected from the group consisting of lower alkyl, halo, nitro, cyano, $-(CH_2)_n-OR^{20}$, $-(CH_2)_n-COOR^{21}$,

$-(CH_2)_n-CONHR^{22}$, $-(CH_2)_n-NHR^{23}$,

25 n is 0, 1, 2, 3 or 4;

R^{20} , R^{21} , R^{22} and R^{23} are independently hydrogen or lower alkyl, and its pharmaceutically acceptable salts thereof.

5. A compound according to any of claims 1 to 4, wherein R^4 is an unsubstituted,
30 mono- or di-substituted five- or six-membered heteroaromatic ring selected from the group consisting of thiazolyl, imidazolyl, oxazolyl, thiadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, or triazinyl.

-134-

6. A compound according to any of claims 1 to 5, wherein R^4 is thiazolyl or pyridinyl, unsubstituted, mono- or di-substituted independently by halogen, lower alkyl or $(CH_2)_n-C(O)OR^{21}$, wherein n is 0, 1 or 2 and R^{21} is lower alkyl.

5

7. A compound according to any one of claims 1 to 3, wherein R^4 is $-C(O)NHR^{16}$, where

R^{16} is hydrogen, lower alkyl, lower alkenyl, hydroxy lower alkyl, $-(CH_2)_n-COOR^{18}$, $-CO-(CH_2)_n-COOR^{19}$;

10 n is 0, 1, 2, 3 or 4;

R^{18} and R^{19} are independently hydrogen or lower alkyl, and its pharmaceutically acceptable salts thereof.

8. A compound according to any of claims 1 to 3 or 7, wherein R^4 is $-C(O)NHR^{16}$,
15 and R^{16} is lower alkyl or lower alkenyl.

9. A compound according to any of claims 1 to 8, wherein R^1 is hydrogen, halo, nitro or cyano.

20 10. A compound according to any of claims 1 to 9, wherein R^1 is hydrogen or halo.

11. A compound according to any of claims 1 to 10, wherein R^2 is hydrogen, halo, nitro, cyano, sulfonamido, lower alkyl, $-OR^5$, $-COOR^5$, perfluoro- lower alkyl, lower alkyl sulfonyl; or

25 R^2 can be $R^{10}-[(CH_2)_y-W]_z-$, where

W is oxygen, sulfur, $-SO-$, or $-SO_2-$, and

R^{10} is a heteroaromatic ring, connected by a ring carbon atom, which contains from 5 to 6 ring members with from 1 to 2 heteroatoms selected from the group consisting of oxygen, sulfur or nitrogen, or

30 aryl containing 6 or 10 ring carbon atoms, or

-135-

aryl containing 6 ring carbon atoms fused with a heteroaromatic ring containing 5 or 6 ring members with 1 or 2 heteroatoms in the ring being selected from the group consisting of nitrogen, oxygen or sulfur, or

a saturated 5- or 6-membered cycloheteroalkyl ring, which contains from 1 to 2

- 5 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, or a cycloalkyl ring having 5 or 6 carbon atoms, or

-NR¹¹R¹², with R¹¹ and R¹² being independently hydrogen or lower alkyl;

y is independently 0,1,2,3 or 4; z is independently 0,1; or

R² can be R¹³-(CH₂)_t-U-, with

- 10 U is -NHCO-, -CONH-, -NHSO₂-, -SO₂NH- and

R¹³ in the same meaning of R¹⁰ and

perfluoro-lower alkyl, lower alkyl, lower alkoxy carbonyl or

-NR¹⁴R¹⁵, R¹⁴ and R¹⁵ are independently hydrogen or lower alkyl; or together with the

nitrogen atom to which they are attached form a five or six-membered heteroaromatic ring

- 15 containing from 1 to 3 heteroatoms selected from sulfur, oxygen or nitrogen;

t is an integer from 0 to 4.

12. A compound according to any of claims 1 to 11, wherein R² is halo, lower alkyl sulfonyl or R¹⁰-[(CH₂)_y-W]_z-.

20

13. A compound according to any of claims 1 to 12, wherein R² is sulfonylmethyl or R¹⁰-[(CH₂)_y-W]_z- where W is SO₂.

14. A compound according to any of claims 1 to 13, wherein the aryl substituent and
25 the group R³ have a syn-relationship.

15. A compound according to any of claims 1 to 14, wherein V is cyclopentyl, cyclohexyl or cycloheptyl.

- 30 16. A compound according to any of claims 1 to 15, wherein V is cyclopentyl or cyclohexyl.

-136-

17. A compound according to any of claims 1 to 14, wherein R³ is isopropyl or n-propyl.

18. A compound according to any of claims 1 to 14, wherein R³ is isobutyl.

5

19. The use of the compounds according to any of claims 1 to 18, or a pharmaceutically acceptable salt thereof, for the treatment or prophylaxis of type II diabetes.

10 20. A pharmaceutical composition comprising a compound of any of claims 1 to 18, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable diluent or carrier.

15 21. The use of a compound according to any of claims 1 to 18, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of type II diabetes.

20 22. A method for the prophylactic or therapeutic treatment of type II diabetes, which comprises administering a compound of any of claims 1 to 18, or a pharmaceutically acceptable salt thereof, to a human being or animal in need thereof.

23. A pharmaceutical composition for treating type II diabetes containing as an active ingredient a compound of any of claims 1 to 18, or a pharmaceutically acceptable salt thereof.

25